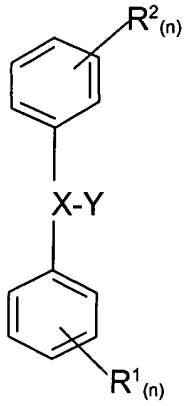
Amendments to the Claims

Claims 1-27: (canceled)

Claim 28. (currently amended): An agent which protects stratified squamous epithelium against injury by a noxious substance, and has the formula:



wherein: X is a linker selected from the group consisting of C_1-C_6 alkylene, C_2-C_6 alkenylene, or C_3-C_6 alkynylene, wherein X may optionally include 1 or 2 oxygen atoms and/or 1 sulfur atom;

Y is a group pendant from X, wherein Y is a C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} akynyl, or aromatic~~, or cyclic aliphatic~~ group to which is attached at least one $-OSO_3R^4$ moiety, and, optionally, at least one OH group, wherein R^4 is H or a pharmaceutically acceptable cation;

[[N]] n is an integer from 1-3; and

R^1 and R^2 are each independently selected from the group consisting of –H, ~~a halogen with an atomic number from 9 to 53,~~ -F, -Cl, -Br, -I, hydroxy, $-SO_3R^4$, $-OSO_3R^4$, -NCS, -NCO, NH(CO)-OR^3, -NH(CS)SR^3, -NH(C=NH)OR^3, $-NHCOCH_2Cl$, $-NHCOCH_2Br$, $-NHCO-CH=CH_2$, $-NHC(O)-CF_3$, $-S-CH_2-CH=CH_2$, $-NHCH_2-C\equiv CH$, $-NH-CH_2-CN$, $-NH-S-CH_2-CH=CH_2$, $-O-CH_2-CH=CH_2$, $-NH-CF_3$, N-mono-. di-, tri-, tetra-, and penta-haloehtyl, -CN, $-NH_2$, $-NO_2$, $-NHCOCH_3$, -CHO, $-COOR^4$, $-N_3$, $-COR^3$, $-R^3OH$, $-R^3NHCOCH_3$, $-R^3OSO_3R^4$, $-OR^3$, $-SR^3$, and $-R^3$, wherein $-R^3$ is p-nitrophenyl, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, if at the distal end of the substituent, or C_1-C_6 alkylene, C_2-C_6 alkenylene, or C_2-C_6 alkynylene, if at the proximal end of the substituent, and wherein R^4 is H or a pharmaceutically acceptable cation.

Claim 29. (currently amended): The agent of claim 28, wherein at least one of ~~R_1 and R_2~~ R^1 and R^2 is -NCS.

Claim 30: (original): The agent of claim 28, wherein X is $-OCH_2-$, or $-CH_2O-$.

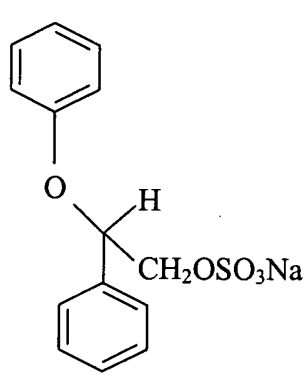
Claim 31. (original): The agent of claim 28, wherein Y is C_1 to C_4 alkyl, to which is attached at least one $-OSO_3R^4$ moiety.

Claim 32. (original): The agent of claim 28, wherein Y is a sulfonated polycarbinol chain of 1 to 6 sulfonated carbon atoms.

Claim 33. (previously presented): The agent of claim 28, wherein at least two $-OSO_3R^4$ moieties are attached to Y.

Claim 34. (original): The agent of claim 28, wherein Y is ethyl-1,2-disulfate.

Claim 35. (previously presented): The agent of claim 28, wherein the agent is selected from the group consisting of:



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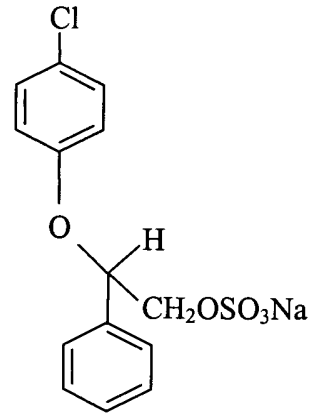

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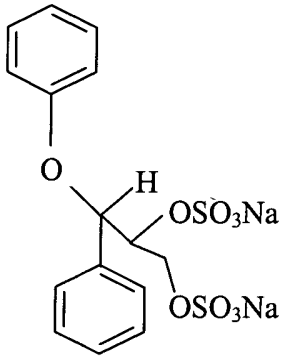

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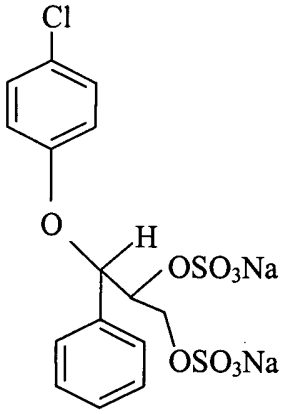

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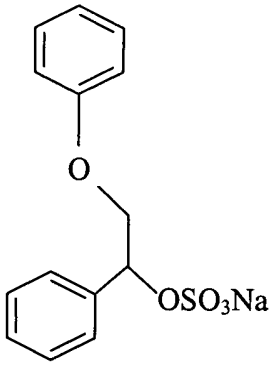

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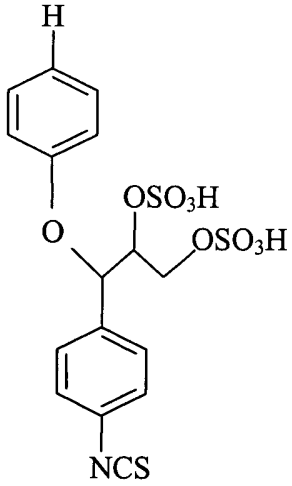

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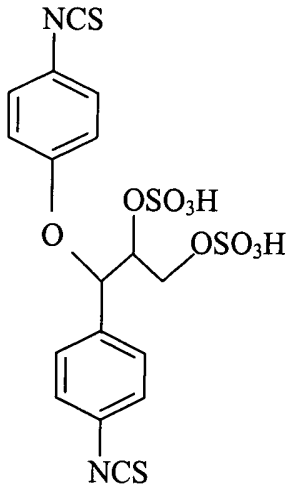
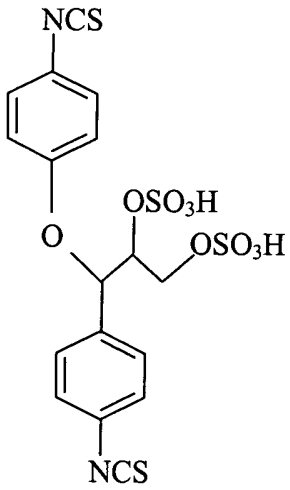


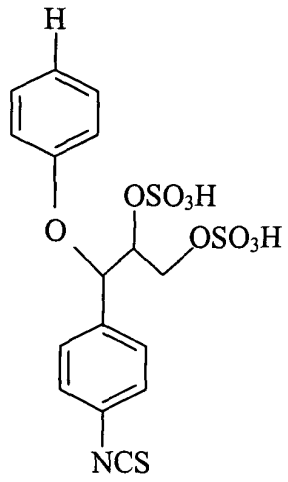
and all pharmaceutically acceptable salts thereof.

Claim 36. (original): The agent of claim 35, wherein the agent is



or a pharmaceutically acceptable salt thereof.

37. (original): The agent of claim 35, wherein the agent is



or a pharmaceutically acceptable salt thereof.

38. (original): A composition comprising an agent according to claim 28 and a pharmaceutically acceptable excipient.

39. (original): A composition comprising an agent according to claim 28 and a proton pump inhibitor.

40. (canceled)

41. (previously presented): The agent of claim 28, wherein from 2 to 6 $-OSO_3R^4$ moieties are attached to Y.

42. (previously presented): The agent of claim 28, wherein Y is C_1-C_6 alkyl, C_2-C_6, alkenyl, or C_3-C_6 alkynyl.

REMARKS/ARGUMENTS

Applicants note that the ownership of this application has transferred from large entity to small entity.

Claims 28-39, 41, and 42 remain in this application. Claim 28 and 29 are hereby amended. Support for the amendment to claim 28 can be found in original claim 28. The amendment to claim 29 is merely to change the subscripts on the "R's" to superscripts to track the structure of claim 28. Claims 1-27 and 40 were previously canceled without prejudice or disclaimer. In view of Examiner's earlier restriction requirement, Applicants retain the right to present claims 1-27 and 40 in a divisional application.

Rejections Under 35 U.S.C. § 112

Claim 28 is rejected under 35 U.S.C. § 112, second paragraph, as indefinite. The phrase "a halogen with an atomic number from 9 to 53" has been changed to recite "-F, -Cl, -Br, and -I." Also in claim 28, the "N" in line 8 after the structure has been changed to "n" to track the structure in the claim.

Applicants respectfully disagree with Examiner's assertion that the term "including" in claim 28, line 2 under the definition of X is indefinite. 35 U.S.C. § 112, second paragraph, is essentially a requirement for precision and definiteness in claim terminology. In re Borkowski, 422 F.2d 904, 164 USPQ 642 (CCPA 1970). Rejection of generic claims under 35 U.S.C. § 112, second paragraph, merely because of breadth is inappropriate. Breadth is not equivalent to indefiniteness. In re Robins, 429 F.2d 452, 166 USPQ 552 (CCPA 1970). Here, Examiner's complaint is that claim 28 is indefinite because X may include elements other than those listed in the claim. This, however, has nothing to do with precision and definiteness of claim terminology. Insofar as claim definiteness is concerned, the Examiner has not pointed out why one of ordinary skill in the relevant art would be unable to determine if a particular chemical compound was, or was not, "an agent which protect stratified squamous epithelium against a noxious substance" as claimed. Accordingly, Examiner has not established that claim 28 lacks the clarity required under 35 U.S.C. § 112, paragraph 2.

Rejections Under 35 U.S.C. § 102(b)

Claim 28 is rejected under 35 U.S.C. § 102(b) as anticipated by Ellison *et al.*, "METABOLISM OF ORPHENADRINE CITRATE IN MAN (Jour. of Pharm. and Exp. Therapeutics) Vol. 176, No. 2, pp. 284-295. The glucuronide/sulfate of *o*-methylbenzhyroloxy acetic acid, or any other compound disclosed in the Ellison article, is not encompassed by amended claim 28. Accordingly, claim 28, as amended, is not anticipated, and therefor patentable over Ellison.

Rejections Under 35 U.S.C. § 103(a)

Claims 28, 29, 31, and 42 are rejected under 35 U.S.C. § 103(a) as unpatentable over Orlando *et al.*, US patents 5,189,056 (hereinafter referred to as '056) and 5,374,537 (hereinafter

referred to as '537), each taken alone. Applicants note that US Pat. No. 5,374,537 is a divisional application of US Pat. No. 5,189,056, and that the specifications of these two patents are identical, except for the statement indicating that '537 is a divisional of '056. Accordingly, Applicants' comments directed to '056 apply equally to '537.

Respectfully, '056 does not teach or suggest the agents of independent claim 28, and claims 29, 31, and 42, which are dependent thereon. '056 does not teach or suggest all of the limitations of claim 28 and the claims dependent thereon. Examiner asserts that the compounds of claims 28, 29, 31, and 42 are obvious as a subgenus of the generic compounds disclosed in '056. "A *prima facie* case of unpatentability requires that the teachings of the prior art suggest *the claimed compounds* to a person of ordinary skill in the art....The prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compound." MPEP § 2144.08A.4. Furthermore, "some motivation to select the claimed species or subgenus must be taught by the prior art." MPEP § 2144.08A.4.(a).

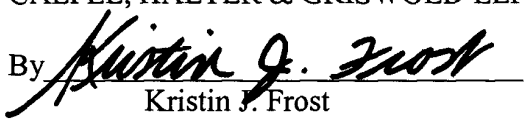
'056 does teach five compounds that have certain features in common with the compounds of claims 28, 29, 31, and 42, such as having two aromatic rings, and some of the substituents that may be on the rings. However, none of the compounds disclosed in '056 have a group pendant to the group linking the two phenyl groups of the disclosed agents, as required in claim 28 and the claims dependent thereon. Nowhere in '056 is there a teaching or suggestion that a pendant group could be added to the linking group. Nothing taught in '056 provides motivation to add a pendant group to the linking group. '056 does not teach or suggest <u>any</u> modifications to the five molecules of its sulfonate class.

Furthermore, Applicants' claimed compounds are not mere homologs of the compounds disclosed in '056—they are different compounds, requiring an additional functional group, *i.e.* a hydrocarbon pendant group containing a sulfonate, which is not taught or suggested in '056. Moreover, not only do none of the compounds disclosed in '056 have a hydrocarbon pendant group on the linking group between the phenyls, none of the compounds disclosed in '056 have any pendent hydrocarbon group at all. Without the requisite teaching, suggestion, or motivation to modify the compounds of '056, particularly, without any teaching, suggestion or motivation to add a hydrocarbon chain containing a sulfonate moiety to the group linking the phenyls, the compounds of the present invention are not obvious over '056 or its corresponding divisional patent '537.

In view of the amendments and remarks made herein, Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

CALFEE, HALTER & GRISWOLD LLP

By 

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